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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

ZARA, JANE J

ART UNIT

PAPER NUMBER

1635

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DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 08/978,637	<b>Applicant(s)</b> RABBANI ET AL.	
	<b>Examiner</b> Jane Zara	<b>Art Unit</b> 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 318-323 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11-6-08</u> .   | 6) <input type="checkbox"/> Other: _____                          |

Continuation of Disposition of Claims: Claims pending in the application are 245,248-251,253-255,260,264,265,268,270,272,284,288-290,296,299,303,304,308-313 and 318-326.

Continuation of Disposition of Claims: Claims rejected are 245,248-251,253-255,260,264,265,268,270,272,284,288-290,296,299,303,304,308-313,325 and 326.

### **DETAILED ACTION**

This Office action is in response to the communication filed 10-15-08.

Claims 245, 248-251, 253-255, 260, 264, 265, 268, 270, 272, 284, 288-290, 296, 299, 303, 304, 308-313, 318-326 are pending in the instant application. Claims 318-323 have been withdrawn as being drawn to non-elected inventions, claims 245, 248-251, 253-255, 260, 264, 265, 268, 270, 272, 284, 288-290, 296, 299, 303, 304, 308-313, 325 and 326 have been examined on their merits as set forth below.

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-15-08 has been entered.

### ***Response to Arguments and Amendments***

#### **Withdrawn Rejections**

Any rejections not repeated in this Office action are hereby withdrawn.

Applicant's arguments with respect to the obviousness rejections have been considered but are moot in view of the new ground(s) of rejection set forth below.

*New Rejections/Rejections Necessitated by Amendments*

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 245, 248-251, 253-255, 260, 264, 265, 268, 270, 272, 284, 288-290, 296, 299, 303, 304, 308-313, 325 and 326 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated multi-cassette nucleic acid construct comprising at least three promoters, and which optionally comprises a nuclear localization sequence comprising a portion of snRNA comprising sequences for at least two stem loops present at the 3' end of native snRNA, a reimportation, and an antisense nucleic acid sequence replacing stem-loop formation of native snRNA, and which nucleic acid construct produces, upon introduction into any eukaryotic cell, at least one specific nucleic acid from each promoter or initiator, which upon insertion into a eukaryotic cell produces more than one specific nucleic acid, each such specific nucleic acid so produced being substantially non-homologous with each other and being either complementary with a specific portion of one or more viral or cellular RNAs in a cell or binds to a specific viral or cellular protein, which virus is optionally HIV, wherein each specific nucleic acid binds to a different target nucleic acid sequence, and the specific

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nucleic acid binds to a specific cellular protein comprising a localizing protein or a decoy protein.

The specification and claims do not adequately describe the various genera comprising i.) any snRNA comprising sequences for stem loops present at the 3' end of any native snRNA, and which comprise any reimportation signal or which comprise any antisense replacing sequences that participated in stem-loop formation in the native form of any snRNA; ii.) any cellular protein comprising any nuclear localizing protein or cytoplasmic localizing protein; iii.) any decoy protein binding to any protein required for viral assembly or viral replication.

The instant disclosure, at the time of filing, does not provide adequate number of species for the broad genera claimed. The specification teaches the human U1 operon, and elimination of 49 base sequence involved in the formation of A and B loops formed by U1. The specification also teaches a three segment, triple operon constructs comprising either three U1 promoters or three T7 promoters, and antisense targeting HIV 5' common leader, the TAT/REV coding sequence and the splice acceptor site for TAT/REV of HIV.

The disclosure of these constructs, however, is insufficient to teach or adequately describe a representative number of species for the broad genera of nucleic acids constructs claimed, such that the common attributes or characteristics concisely identifying members of each proposed genus are exemplified, and further whereby any primary nucleic acid construct comprising any primary nucleic acid sequence is introduced into any eukaryotic cells and acts as a template for the synthesis of any

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secondary nucleic acid for the synthesis of any gene product, which nucleic acid construct comprises any snRNA comprising sequences for stem loops present at the 3' end of any native snRNA, and which comprise any reimportation signal or which comprise any antisense replacing sequences that participated in stem-loop formation in the native form of any snRNA; ii.) any cellular protein comprising any nuclear localizing protein or cytoplasmic localizing protein; iii.) any decoy protein binding to any protein required for viral assembly or viral replication. The general knowledge and level of skill in the art at the time of filing do not supplement the omitted description because specific, not general, guidance is what is needed to provide a representative number of species for the broad array of nucleic acid constructs claimed.

Since the disclosure and the prior art, at the time of filing, fail to describe the common attributes or characteristics concisely identifying members of the proposed genera of compounds claimed, or fail to provide an adequate number of species for the broad genera claimed, the description provided for this very broad genera of compounds is insufficient. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the very broad genera claimed.

Thus, applicant was not in possession of the claimed genera.

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***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 245, 248-251, 253-255, 260, 264, 299, 303, 304, 308-313, 325, 326 are rejected under 35 U.S.C. 103(a) as being unpatentable over Calabretta et al. (USPN 5,734,039), in view of Binkley et al. (Nucleic Acids Research, 1995, Vol. 23, No. 16, pages 3198-3205), the combination further in view of Craig et al. (WO 95/08635) and Alul et al (USPN 5,532,130) insofar as the claims are drawn to an isolated multi-cassette nucleic acid construct comprising three promoters, which upon insertion into a eukaryotic cell produces more than one specific nucleic acid, each such specific nucleic acid so produced being substantially nonhomologous with each other and being either complementary with a specific portion of one or more viral or cellular RNAs in a cell or binds to a specific viral or cellular protein, wherein each specific nucleic acid binds to different target nucleic acid sequences, wherein the specific nucleic acids bind to a specific cellular protein comprising a localizing protein or a decoy protein, which virus is optionally HIV.

Calabretta et al. teach a composition for introducing two different antisense oligonucleotides specific for two different genes to a cell. Calabretta et al. teach a nucleic acid construct comprising a first promoter segment and a segment containing DNA of a cytoplasmic oncogene or proto-oncogene DNA, and a second promoter



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segment and a segment containing DNA of a nuclear oncogene or proto-oncogene.

The DNA containing segments are in inverted orientation such that transcription of the DNA produces RNA complementary to the two mRNA transcripts of the two oncogene targets (see columns 8 and 9, for example). Calabretta et al. teach various modifications of the nucleic acids and teach means of delivery of the compositions.

Binkley et al. teach high affinity RNA ligands to human nerve growth factor (NGF), which is a protein that is essential for growth, differentiation and maintenance of neurons and has the ability to localize or attract NGF-sensitive growing axons. Binkley et al. teach that the SELEX procedure is a widely used technique for isolating, identifying, and characterizing RNAs with high specificity and affinity to proteins. Binkley et al. teach that specific RNA ligands to proteins can be isolated using SELEX.

The primary references do not teach nucleic acids that bind to or target nucleic acids encoding HIV cellular proteins, nor that bind to decoy proteins.

Craig et al. teach the expression of viral decoy proteins under the control of a locus control region and teach that decoy proteins act as antagonists to natural proteins involved in the replication of the HIV virus. Craig et al. teach that a decoy protein can be used as a mutant of a transactivator protein that is capable of binding to the transactivator-responsive site on the host or viral genome, yet is incapable of activating transcription (see pages 2 and 3, for example).

Alul et al teach the routine experimentation and design of antisense or ribozymes to target HIV RNA encoding proteins (see esp. the second paragraph of the section entitled "Background of the Invention."

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It would have been obvious to incorporate RNA oligonucleotides that bind to proteins, as taught by Binkley et al. in place of the antisense oligonucleotides taught in the system of Calabretta et al. One would have been motivated to incorporate RNA oligonucleotides that bind to proteins instead of the antisense oligonucleotides in the system of Calabretta et al. because Binkley et al. teach that high affinity RNA ligands to proteins, such as NGF that localizes NGF-sensitive growing axons, can be easily isolated using the SELEX procedure and teach that such RNAs may furnish useful diagnostic tools for the study of proteins. Since both types of nucleic acid oligonucleotides are used to determine binding interactions, as evidenced by the teachings of Calabretta et al. and Binkley et al., one would have been motivated to express the RNA ligands taught by Binkley et al. in the system of Calabretta et al. One would have a reasonable expectation of success given that each of the nucleic acid molecules were known to bind with target molecules in a sequence specific manner, as evidenced by Calabretta et al. and Binkley et al. One would have a reasonable expectation of success to express the protein binding RNA molecules of Binkley et al. in the dual system of Calabretta et al., with the advantage of producing two different binding molecules at once.

It also would have been obvious to use the SELEX method to assay for RNA molecules that bind to a protein, as taught by Binkley et al. and to specifically use a decoy protein as the protein, as taught by Craig et al. One of ordinary skill would have been motivated to design and synthesize antisense that target and inhibit HIV proteins because in the search for potential therapeutics to inhibit HIV infections, as taught

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previously by many in the art, including Alul et al. One would have been motivated to screen for resultant RNA aptamers against a decoy protein because Binkley et al. teach that high affinity RNA ligands to proteins can be easily isolated using the SELEX procedure and teach that such RNAs may furnish useful diagnostic tools for the study of proteins. Since Craig et al. teach that decoy proteins are proteins that are useful to serve as a mutant that is capable of binding to a preferred site but yet is incapable of activating transcription, one would have been motivated to use the SELEX method of Binkley et al. to identify RNA ligands to any known protein, such as the decoy proteins of Craig et al.

One would have a reasonable expectation of success given that Craig et al. teach the benefits of decoy proteins and Binkley et al. teach assaying for RNA aptamers to proteins and teach a method (SELEX) that is widely use to identify RNA molecules that bind to known proteins.

Thus, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments and declaration filed 10-15-08 have been fully considered but they are not persuasive. Applicant argues that the instant invention would not have been obvious because Calabretta has not mention of whether multivalent or separate transcripts would be of use and with regard to cytoplasmic targets. Applicant also argues that the second promoter in Calabretta is not to increase the number of transcripts per se but to add additional properties for targeting different genes, And Calabretta does not suggest any utility of having more than two cited operons.

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Applicant is arguing limitations that simply do not exist in the claims. Calabretta is properly relied upon for teaching the routine use of multi-promoter constructs for expressing different nucleic acid constructs. The problem of mutability that is addressed by the instant disclosure, as suggested by Applicants, is not a limitation that is presently claimed. And, contrary to Applicant's assertions, it would have been obvious to construct a nucleic acid construct with more than two different promoters driving expression of different gene products. This would have involved nothing more than routine experimentation at the time of the instant invention, and relying on the prior teachings of Calabretta and ALul et al for the utilizing these constructs to target HIV RNA.

### ***Conclusion***

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's

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supervisor, James (Douglas) Schultz, can be reached on (571) 272-0763. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**Jane Zara**  
**1-2-09**

/Jane Zara/

Primary Examiner, Art Unit 1635